

IN THE CLAIMS:

Claims 1, 2, 5, 12, 13, 21, 22, 24, 31-34, 37, 43, 44, 46, 48, 55, 56, 62, and 63 have been amended herein. New claim 64 is presented herein. All of the pending claims 1-64 are presented below. This listing of claims will replace all prior versions and listings of claims in the application. Please enter these claims as amended.

Listing of the Claims:

1. (Currently Amended) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species, said *thyA* mutant comprising:

~~a defective~~ a nucleic acid encoding an inactive *Lactococcus* thymidylate synthase gene;
wherein said strain of *Lactococcus* species comprises a thymidylate synthase gene comprising
at least 100 contiguous nucleotides that are at least 90% identical to a region of SEQ ID
NO: 1; and
at least 100 contiguous nucleotides that are at least 90% identical to a region of SEQ ID
NO: 2.

2. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 1, wherein said ~~defective~~ inactive *Lactococcus* thymidylate synthase ~~gene~~ has been inactivated by gene disruption.

3. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 1, wherein the *Lactococcus* species is *Lactococcus lactis*.

4. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 2, wherein the *Lactococcus* species is *Lactococcus lactis*.

5. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 1, wherein said (*thyA*) mutant is further transformed with a transforming plasmid,

wherein said transforming plasmid does not ~~comprise an functional~~ encode an active thymidylate synthase ~~gene~~.

6. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 5, further comprising a gene encoding a molecule of interest.

7. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 5, wherein said molecule of interest is Interleukin-10.

8. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 5, wherein said *Lactococcus* species is *Lactococcus lactis*.

9. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 8, wherein the *Lactococcus lactis* comprises a gene encoding a molecule of interest.

10. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 9, wherein the molecule of interest is Interleukin-10.

11. (Withdrawn) A method for delivering a molecule of interest to a subject, said method comprising administering the transformed strain of *Lactococcus* species of claim 6 to the subject.

12. (Currently Amended) A composition comprising:
the isolated thymidylate synthase (*thyA*) mutant ~~of a strain of a *Lactococcus* species~~ of claim 5.

13. (Currently Amended) The composition of claim 12, wherein the isolated thymidylate synthase (*thyA*) mutant ~~of a strain of *Lactococcus* species~~ further comprises a gene encoding a molecule of interest.

14. (Original) The composition of claim 13, wherein said molecule of interest is Interleukin-10.

15. (Original) The composition of claim 12, wherein said *Lactococcus* species is *Lactococcus lactis*.

16. (Original) The composition of claim 15, wherein the *Lactococcus lactis* comprises a gene encoding a molecule of interest.

17. (Original) The composition of claim 16, wherein the molecule of interest is Interleukin-10.

18. (Withdrawn) A method of treating inflammatory bowel disease in a subject, said method comprising:
administering to the subject a transformed strain of *Lactococcus* species of claim 6.

19. (Withdrawn) The method of claim 18, wherein the molecule of interest is Interleukin-10.

20. (Withdrawn) A method for delivering a molecule of interest to a subject, said method comprising administering the transformed strain of *Lactococcus* species of claim 9 to the subject.

21. (Currently amended) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* bacterium, said *thyA* mutant comprising:

~~a genome, and, incorporated into said genome, a strain of *Lactococcus* bacterium; and~~
a means for encoding ~~a defective~~ an inactive *Lactococcus* thymidylate synthase gene; and
wherein said means for encoding an inactive *Lactococcus* thymidylate synthase is incorporated into the genome of said strain of *Lactococcus* bacterium

~~wherein said genome has been genetically modified through introducing a defect in said *thyA* thymidylate synthase gene.~~

22. (Currently Amended) ~~The isolated thymidylate synthase (*thyA*) mutant of claim 21;~~ An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* bacterium, said *thyA* mutant comprising:

a strain of *Lactococcus* bacterium; and
a means for encoding an inactive *Lactococcus* thymidylate synthase wherein said means for encoding an inactive *Lactococcus* thymidylate synthase is incorporated into the genome of said strain of *Lactococcus* bacterium; and

wherein said strain of *Lactococcus* bacterium comprises a ~~thymidylate synthase gene~~ a nucleotide sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

23. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 21, wherein the *Lactococcus* bacterium is a *Lactococcus lactis* bacterium.

24. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of claim 21, further comprising a transforming plasmid; and

wherein said transforming plasmid does not ~~comprise an functional~~ encode an active thymidylate synthase ~~gene~~.

25. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 24, further comprising a gene encoding a molecule of interest.

26. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 25, wherein said molecule of interest is Interleukin-10.

27. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 24, wherein said *Lactococcus* bacterium is a *Lactococcus lactis* bacterium.

28. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 27, wherein the *Lactococcus lactis* bacterium comprises a gene encoding a molecule of interest.

29. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 28, wherein the molecule of interest is Interleukin-10.

30. (Previously Presented) A composition comprising: the isolated thymidylate synthase (*thyA*) mutant of claim 21.

31. (Currently Amended) The isolated *thyA* mutant of a strain of *Lactococcus* species of claim 1, wherein said ~~strain of *Lactococcus* species~~ nucleic acid encoding an inactive *Lactococcus* thymidylate synthase comprises a thymidylate synthase gene a nucleotide sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

32. (Currently Amended) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species, wherein said *thyA* mutant comprises a nucleic acid encoding an inactive

Lactococcus thymidylate synthase, and wherein said *thyA* mutant produced by a process comprising:

providing a strain of *Lactococcus* species comprising a thymidylate synthase gene comprising

at least 100 contiguous nucleotides that are at least 90% identical to a region of SEQ ID NO: 1; and

at least 100 contiguous nucleotides that are at least 90% identical to a region of SEQ ID NO:2; and

~~introducing a defect in~~ altering said *Lactococcus* thymidylate synthase gene to inactivate the thymidylate synthase encoded thereby.

33. (Currently Amended) The isolated *thyA* mutant of a strain of *Lactococcus* species according to claim 32, wherein said *Lactococcus* thymidylate synthase gene is comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5 ~~and introducing a defect in said thymidylate synthase gene.~~

34. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 32, wherein ~~said defective~~ altering said *Lactococcus* thymidylate synthase gene to inactivate the *Lactococcus* thymidylate synthase encoded thereby ~~has been inactivated~~ comprises by gene disruption.

35. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 32, wherein the *Lactococcus* species is *Lactococcus lactis*.

36. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 34, wherein the *Lactococcus* species is *Lactococcus lactis*.

37. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 32, wherein said (*thyA*) mutant is transformed with a transforming plasmid,

wherein said transforming plasmid does not ~~comprise an intact~~ encode an active thymidylate synthase ~~gene~~.

38. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 37, further comprising a gene encoding a molecule of interest.

39. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 37, wherein said molecule of interest is Interleukin-10.

40. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 37, wherein said *Lactococcus* species is *Lactococcus lactis*.

41. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 40, wherein the *Lactococcus lactis* comprises a gene encoding a molecule of interest.

42. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 41, wherein the molecule of interest is Interleukin-10.

43. (Currently Amended) An isolated thymidylate synthase (*thyA*) mutant of a *Lactococcus* bacterium, said *thyA* mutant comprising a ~~defective~~ *Lactococcus* thymidylate synthase gene, wherein said ~~defective~~ *Lactococcus* thymidylate synthase gene has been

genetically modified through introducing a defect in said *Lactococcus* thymidylate synthase gene which inactivates the *Lactococcus* thymidylate synthase encoded therein.

44. (Currently Amended) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 43, wherein ~~the defective thymidylate synthase gene has been inactivated by~~ wherein introducing said a defect in said *Lactococcus* thymidylate synthase gene which inactivates the *Lactococcus* thymidylate synthase encoded thereby comprises gene disruption.

45. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 43, wherein the *Lactococcus* bacterium is a *Lactococcus lactis* bacterium.

46. (Currently Amended) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 43, further comprising a transforming plasmid; and wherein said transforming plasmid does not ~~comprise an intact~~ encode an active thymidylate synthase gene.

47. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 46, further comprising a gene encoding a molecule of interest.

48. (Currently Amended) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 47, wherein said gene encoding a molecule of interest is integrated within the ~~defective~~ *Lactococcus* thymidylate synthase gene.

49. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 47, wherein said gene encoding a molecule of interest replaces a part of or the entire thymidylate synthase gene of said *Lactococcus* bacterium.

50. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 48, wherein said molecule of interest is a prophylactic or therapeutic molecule.

51. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 49, wherein said molecule of interest is a prophylactic or therapeutic molecule.

52. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 47, wherein said molecule of interest is Interleukin-10.

53. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 46, wherein said *Lactococcus* bacterium is a *Lactococcus lactis* bacterium.

54. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 53, wherein the *Lactococcus lactis* bacterium comprises a gene encoding a molecule of interest.

55. (Currently Amended) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 54, wherein said gene encoding a molecule of interest is integrated within the ~~defective~~ *Lactococcus* thymidylate synthase gene.

56. (Currently amended) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 54, wherein said gene encoding a molecule of interest replaces a part of or the entire *Lactococcus* thymidylate synthase gene of said *Lactococcus* bacterium.

57. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 55, wherein said molecule of interest is a prophylactic or therapeutic molecule.

58. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 56, wherein said molecule of interest is a prophylactic or therapeutic molecule.

59. (Previously Presented) The isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 54, wherein the molecule of interest is Interleukin-10.

60. (Previously Presented) A composition comprising the isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 43.

61. (Previously Presented) A pharmaceutical composition comprising the isolated *thyA* mutant of a *Lactococcus* bacterium according to claim 43.

62. (Currently Ameded) An improvement in an isolated *Lactococcus* bacterium comprising SEQ ID NO:3 or SEQ ID NO5, wherein the improvement comprises:

~~a defect in~~ altering SEQ ID NO:3 or SEQ ID NO:5 to inactivate the *Lactococcus* thymidylate synthase encoded thereby.

63. (Currently Amended) An improvement in an isolated *Lactococcus* bacterium comprising SEQ ID NO:3 or SEQ ID NO:5, wherein the improvement comprises:

~~a defective~~ altering a *Lactococcus* thymidylate synthase gene of said isolated *Lactococcus* bacterium to encode an inactive thymidylate synthase.

64. (New) A recombinant *Lactococcus* strain, with environmentally limited growth and viability comprising a genetically modified mutant of *Lactococcus* bacterium, wherein the mutant expresses a recombinant protein of interest, but lacks any *Lactococcus* thymidylate synthase activity.